"ORAL AND GASTROINTESTINAL MICROBIOME DYSBIOSIS AND ORAL HEALTH: RATE OF ENDOGENOUS ETHANOL PRODUCTION AS A SIMPLE BIOMARKER"

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ABSTRACT

Background: The natural production of small amounts of ethanol within the human body has intrigued scientists for over a century. In studying EnEth, it is crucial to use multiple independent methods of alcohol analysis or detect ethanol in more than one bodily fluid to ensure accuracy.

Aim: This study aimed to evaluate and compare endogenous blood and salivary ethanol concentrations in healthy controls and patients with periodontal diseases, analyzing their correlation with demographic, anthropometric, and oral health parameters.

Methodology: A comparative analysis was conducted between healthy controls and study group participants with periodontal disease. Demographic, anthropometric, and oral health parameters were recorded, and serum and salivary ethanol levels were analyzed across age, gender, body mass index (BMI), waist circumference, and DMFT index. Diagnostic accuracy was evaluated using Receiver Operating Characteristic (ROC) curve analysis.

Results: The study revealed significant differences between the control and study groups in demographic, anthropometric, and oral health parameters. The study group had a higher mean age (34.98 ± 11.31 years, $P = 0.033$), BMI (24.97 ± 4.78, $P = 0.015$), and waist circumference (91.58 ± 14.30 cm, $P < 0.001$) compared to controls. While gender distribution was similar ($P = 0.999$), the study group exhibited higher prevalence rates of fluorosis (3.8%), dental erosion (1.9%), and oral mucosal lesions (1.9%). The mean DMFT score was also significantly higher in the study group (5.09 ± 5.50), with 81.1% having DMFT > 0. Both serum (0.06 ± 0.018 μM/mL, $P < 0.001$) and salivary (0.033 ± 0.02 μM/mL, $P = 0.005$) ethanol levels were elevated in the study group, showing significant differences across age, BMI, and DMFT categories. A moderate correlation ($r = 0.286$, $P = 0.003$) between serum and salivary ethanol levels was observed, stronger in controls ($r = 0.398$) than the study group ($r = 0.058$). ROC analysis demonstrated that serum ethanol levels (AUC = 0.857) had superior diagnostic accuracy compared to salivary ethanol levels (AUC = 0.633).

Conclusion: Serum ethanol levels demonstrate higher diagnostic accuracy compared to salivary ethanol levels, making them a reliable marker for distinguishing between groups. The findings underscore significant differences in anthropometric and oral health parameters, correlating with elevated ethanol biomarkers. Further research is warranted to validate salivary ethanol as a non-invasive diagnostic tool.

1. INTRODUCTION

1.1. Endogenous Ethanol (EnEth)

Ethanol, commonly known as alcohol, is one of the oldest beverages and plays a significant role in social life worldwide. Beyond exogenous consumption, the body can produce ethanol endogenously through metabolic pathways, a phenomenon known as auto-brewery syndrome (ABS) or gut fermentation syndrome. In ABS, ethanol concentrations can reach levels sufficient to mimic alcohol intoxication despite little to no alcohol consumption [1].

ABS occurs when fungi or bacteria in the gastrointestinal system, or oral cavity ferment carbohydrates into ethanol, often after carbohydrate-rich meals or antibiotic use. The most common causative organisms are yeasts like *Saccharomyces cerevisiae* and *Candida albicans*, though bacteria such as *Klebsiella pneumoniae* and *Enterococcus faecalis* have also been implicated in ABS. The process involves anaerobic fermentation of carbohydrates, producing acetaldehyde, which is then converted to ethanol by microbial alcohol dehydrogenase (ADH) [1].

Figure 1 shows the illustration of biosynthesis and clearance of endogenous ethanol and acetaldehyde [2].

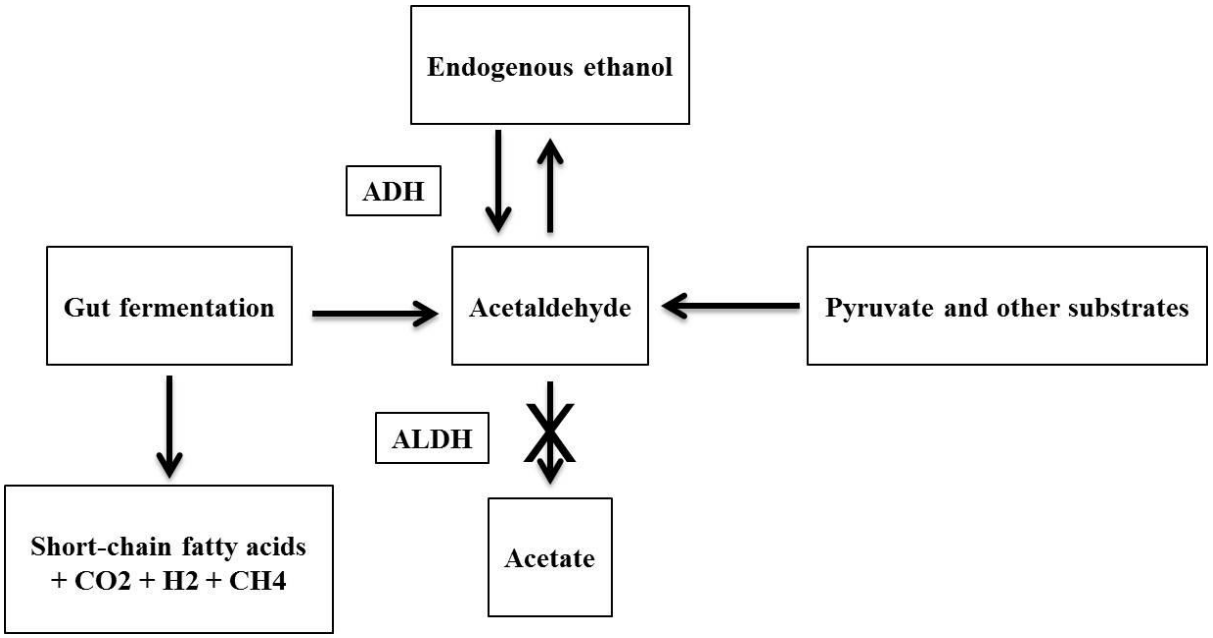


Figure 1. Illustration of biosynthesis and clearance of endogenous ethanol and acetaldehyde

Under theoretical conditions where ethanol is produced in the gut via microbial fermentation of carbohydrates, it enters the portal venous blood, passes through the liver, and undergoes metabolism before reaching systemic circulation. The liver efficiently detoxifies ethanol via first-pass metabolism, capable of oxidizing 6–8 g of ethanol per hour through enzymatic pathways. Only ethanol exceeding this rate can accumulate in the body. At low portal blood ethanol concentrations, the hepatic ADH ensures effective clearance, with residual ethanol diluted in the total body water (50–60% of body weight) [2].

Ongoing research highlights genetic, metabolic, and microbial factors influencing EnEth production [3]. Studies confirm that the gastrointestinal flora is the primary source of EnEth, producing both ethanol and acetaldehyde [3]. Non-microbial pathways, such as carbohydrate metabolism, also contribute to small amounts of EnEth [2]. Factors like aldehyde dehydrogenase (ALDH) deficiency, prevalent in about 50% of the Japanese population, exacerbate acetaldehyde accumulation, triggering symptoms like flushing, headaches, and confusion. Candida species, possessing pyruvate decarboxylase, can ferment carbohydrates into acetaldehyde, leading to further ethanol synthesis in ALDH-deficient individuals. This process is amplified by gut dysbiosis, hypoacidity, or stagnation of carbohydrates in the gastrointestinal tract [4]. ABS is associated with conditions like gastrointestinal disorders (e.g., Crohn's disease), type 2 diabetes, liver cirrhosis, and non-alcoholic fatty liver disease. It can also occur in healthy individuals under certain conditions like gut dysbiosis or hypoacidity. Additionally, studies comparing ABS patients to healthy cohorts reveal unique lifestyle and health patterns, such as reduced sleep, higher prevalence of allergies, and dietary differences. Stress and meal skipping may exacerbate symptoms [3]. While rare, ABS highlights the complexity of human microbiota in influencing systemic health and underscores the importance of recognizing endogenous ethanol production as a clinical condition [3].

Advances in analytical techniques, such as gas chromatography and mass spectrometry, have significantly enhanced the sensitivity and specificity of EnEth detection [5]. In healthy individuals, blood ethanol levels generally range from 0 to 0.7 mmol/L remaining well below thresholds associated with legal intoxication [1]. This suggests that baseline EnEth levels in the general population are typically low, despite speculation about potential variability. Research highlights conditions where EnEth production is markedly increased. For instance, a recent study reported significantly elevated ethanol concentrations in diabetic patients (4.85 ± 3.96 mg/dL) and patients with liver cirrhosis (3.45 ± 2.65 mg/dL) compared to a control group (0.3 ± 0.41 mg/dL) [6]. Such findings underline the role of metabolic and systemic diseases in influencing EnEth levels.

1.2 Microbiology of the Oral Cavity

The oral microbiome, the second-most complex microbial community after the gut, hosts around 700 microbial species despite challenges like fluctuating pH, nutrient levels, and mechanical forces [7]. Key oral habitats include the mucosa, tongue dorsum, and dental surfaces. Healthy oral microbiota maintain balance, while dysbiosis - a shift favouring pathogenic microbes—leads to disease [7].

The Human Microbiome Project and the Human Oral Microbiome Database have revealed that the oral microbiome exhibits high within-individual (α) diversity and low between-individual (β) diversity, indicating a relatively consistent microbial composition across individuals [8]. Supra- and sub-gingival plaques are among the most diverse bacterial habitats in the oral cavity, displaying significant microbial richness. Despite its taxonomic variability, the oral microbiome remains functionally consistent and is predominantly composed of phyla such as *Firmicutes, Bacteroidetes,* and *Fusobacteria,* reflecting its role in maintaining oral health and systemic balance [8].

Periodontal disease (PD) is a general term encompassing a group of inflammatory pathologies that mainly include gingivitis and periodontitis. It is one of the most prevalent inflammatory conditions affecting adults, often leading to tissue and bone loss, tooth loss, and a reduced quality of life. In 2010, it was reported that 3.9 billion people worldwide were affected by this condition [9]. Unlike most infections, periodontitis arises from an imbalance of oral microbes rather than external pathogens. Increased microbial load and shifts toward pathogenic taxa (*Porphyromonas gingivalis, Tannerella forsythia* and *Treponema denticola,* etc.) drive disease progression [7].

The oral microbiome plays a significant role in systemic health and has been implicated in various conditions, including cardiovascular diseases like atherosclerosis, neurological disorders such as Alzheimer's disease, endocrine and metabolic conditions like diabetes and obesity, as well as respiratory diseases and adverse pregnancy outcomes. These associations are primarily driven by mechanisms such as bacteraemia, immune system activation, and the dissemination of oral pathogens to non-oral sites, including their presence in atheromatous plaques, highlighting the far-reaching impact of oral microbial imbalances on overall health [9].

Gap of knowledge - Need for the Study

The natural production of small amounts of ethanol within the human body has intrigued scientists for over a century. In studying EnEth, it is crucial to use multiple independent methods of alcohol analysis or detect ethanol in more than one bodily fluid to ensure accuracy. Considering this, the present study aimed to evaluate EnEth levels in the blood and saliva of participants. The variation in EnEth concentrations between saliva and blood, particularly in relation to oral diseases, could serve as a valuable, cost-effective, non-invasive, and easily accessible biological parameter. This marker may offer insights into disease severity, prognosis, or potential targets for intervention. If confirmed, the findings could establish a new framework for understanding the interplay between the oral and gut microbiomes and oral diseases, positioning EnEth as a crucial tool in biomarker research and analysis.

This study is the first worldwide to assess whether dysbiosis in the oral and gut microbiomes can alter EnEth levels, as measured in saliva and peripheral blood using sensitive enzymatic colorimetric methods, in relation to oral health, particularly PD, as hypothesized. If confirmed, the findings would suggest a new paradigm for understanding the relationship between the oral/gastrointestinal microbiome and oral diseases, making the measurement of EnEth a simple, cost-effective tool in biomarker analysis.

2. AIM AND OBJECTIVES

2.1. General Objective

To evaluate and compare endogenous blood and salivary ethanol concentrations in patients with periodontal diseases and correlate them with demographics, anthropometrics, and oral status.

2.2. Specific Objectives

a. To quantitatively evaluate endogenous blood and salivary ethanol concentrations in apparently general and oral healthy controls;
b. To evaluate endogenous blood and salivary ethanol concentrations in patients with periodontal diseases;
c. To compare endogenous blood and salivary ethanol concentrations among the two groups and correlate these changes with demographics, anthropometrics, and oral status of the participants; and
d. Evaluate the biomarker potential of EnEth to differentiate healthy controls from patients.

3. RESEARCH QUESTION

Do endogenous blood and salivary ethanol levels correlate with oral health status, and can they differentiate patients from healthy controls?

Null Hypothesis

There is no significant difference in endogenous blood and salivary ethanol concentrations between patients with periodontal diseases and healthy controls, and these concentrations neither have biomarker potential nor have significant correlation with demographics, anthropometrics, or oral status of patients.

4. REVIEW OF LITERATURE

4.1. EnEth

4.1.1. Historical Background

EnEth production was first reported in 1948 by Ladkin and Davies in a 5-year-old African boy with gastrointestinal issues. Research identified genetic predispositions, such as defective ALDH in Japanese populations, but cases have been documented across ethnicities [10,11].

4.1.2. Mechanisms of EnEth Production

In healthy individuals, gut flora produces ethanol metabolized by liver enzymes. Factors like antibiotic use, liver dysfunction, diabetes, and Crohn's disease can impair metabolism, leading to ABS [12]. Candida species and Saccharomyces cerevisiae are primary contributors, with Candida converting glucose to ethanol efficiently [12]. Elevated ethanol levels are linked to gut microbiota imbalances, genetic differences, and specific health conditions [12]. Some studies suggest bacterial involvement, with probiotics potentially altering gut flora [12].

4.1.3. Measurement of EnEth

Methods to detect EnEth in blood and urine include:

a. *Gas Chromatography-Mass Spectrometry (GC-MS):* Highly sensitive and specific, detecting levels as low as 0.05 mg/L [13].
b. *Headspace Gas Chromatography (HS-GC):* Effective in diabetes and population studies, revealing elevated ethanol levels in conditions like obesity [1].
c. *ADH Assays:* Useful for screening but prone to interference [14].

d. *Gas-Liquid Chromatography (GLC):* Accurate for biological fluids, linking altered gut motility to ethanol production [14].

Studies highlight variability in EnEth levels due to health, genetics, and analytical methods, emphasizing the need for precise detection techniques [13,14].

4.2. Periodontal Disease and Microbial Dysbiosis

4.2.1. Definition and Pathogenesis

PD arises from microbial imbalances in the oral cavity, dominated by Gram-negative anaerobic bacteria like *Porphyromonas gingivalis*, *Treponema denticola*, and *Tannerella forsythia* ("red complex") [15]. These pathogens colonize enamel and gingival margins, triggering immune responses via Toll-like receptors on periodontal epithelial and connective tissue cells [15]. This leads to the release of inflammatory mediators (e.g., TNF-α, IL-1β, RANK-L), promoting osteoclastogenesis, bone resorption, and clinical attachment loss (CAL). Chronic infection amplifies inflammation, potentially spreading systemically through microbial translocation or circulating mediators [15].

4.2.2. Systemic Implications of Periodontal Disease

PD is linked to systemic conditions like diabetes, cardiovascular disease, rheumatoid arthritis, and non-alcoholic fatty liver disease (NAFLD) [16]. Oral-gut interactions play a key role, as periodontopathic bacteria can colonize the gut, disrupting microbial balance and exacerbating dysbiosis [16]. This bidirectional relationship highlights the need for integrated oral-systemic health management to prevent widespread inflammation and disease progression.

5. MATERIALS AND METHODS

5.1. Study Design: A quantitative, analytical, cross-sectional, case-control study.

5.2. Ethical Clearance: Ethical approval was obtained from the Local Permanent Committee for Research Ethics, Jouf University, Sakaka, Saudi Arabia (Approval# 10-07/41).

5.3. Study Duration: January 2021 to November 2023.

5.4. Sample Size Estimation

Sample size estimation was done by using GPower software ((version 3.0, Heinrich-Heine-University, Düsseldorf, Germany). Sample size was estimated for F test and ANOVA: Omnibus fixed one way, for 2 groups with equal sample size was chosen. A minimum total sample size of 106 (53 per group) was found to be sufficient for an alpha of 0.05,

power of 80%, 0.25 as effect size (assessed for difference in ethanol levels). Participants were randomized by sequential enrollment in each group till the sample size was satisfied.

5.5. Sample Selection and Characteristics

The inclusion criteria considered was- i) Volunteering and informed consented adult participants' aging ≥20 years; ii) no diagnosed systemic chronic or inflammatory disease; and iii) have received no treatment for the oral lesion in last 6 months. The exclusion criteria considered was- i) pregnant and lactating patients; ii) any history of tobacco and tobacco-related products or alcoholism; and iii) taken antibiotics or anti-inflammatory drugs within one month prior to the study.

The selected patients were properly briefed and signed consent before starting the study.

5.6. Procedure

5.6.1. Oral Examination

World Health Organization (WHO) Oral Health Assessment Form for Adults (2013) [17] was used to assess the oral status of the participants. Proper record of the clinical data was maintained at the first visit for each participant.

5.6.1.1. Periodontal status

For each patient, complete oral and periodontal examination was performed. The periodontal status was evaluated based on various criteria as included in WHO Oral Health Assessment Form for Adults (2013) [17]. The assessment was conducted using a standardized periodontal probe.

5.6.1.2 Decay, Missing and Filled indices (DMFT) score

The WHO criteria (2013) [17] were used to record dental caries experience using the DMFT for permanent dentition. The presence or absence of each tooth was recorded and, for each missing tooth, the participant's information for the underlying reason (e.g., decay, trauma, periodontics-related extraction, periodontal disease) was recorded. A tooth was considered missing only when it had been extracted because of dental caries.

5.6.1.3 Other oral conditions or lesions

Based on the clinical findings, the selected participants were divided into 2 major groups (n = 53 per group) as follow:

- **Control group:** Clinically healthy individuals with mean BOP < 20% of sites, no sites with PPD ≥ 3 mm, and no CAL, and DMFT score = 0; and
- **Study group:** Participants with PD with mean BOP > 20% of sites, sites with PPD ≥ 3 mm and CAL ≥ 2 mm, and DMFT score ≥ 1.

5.6.2 Anthropometric Measurements

Anthropometric measurements included body mass index (BMI) and waist circumference. BMI was calculated as weight (kg) divided by height (m^2), classifying individuals as malnourished (BMI<18.5), normal (18.5–24.9), overweight (≥25), or obese (≥30). Waist circumference was measured with a flexible tape at the midpoint between the umbilical scar and the inferior rib border while standing. Thresholds for health risks were set at ≥88 cm for women and ≥102 cm for men [18].

5.6.3. Sampling and Biochemical Assay of EnETh

5.6.3.1. Blood Collection, Storage and Processing

For EnEth analysis, morning blood sample were taken from cubital vein after overnight fasting by a trained nurse. Disinfection of cubital region was performed by 3% hydrogen peroxide, and then by sterile distilled water. 2.0 mL of peripheral blood sample were collected aseptically on sterile EDTA blood collection tubes from each participant. Plasma was recovered by centrifugation at 5000 rpm for 10 minutes at 4°C. Plasma was aliquot (0.250 µL each) stored at -60°C prior to analysis.

5.6.3.2. Saliva Collection, Storage and Processing

Participants were asked not to eat, drink or brush their teeth in the morning of the collection day. Unstimulated whole-mouth saliva was collected by expectoration into sterilized universal tubes, over a period of 5 minutes with the patient sitting in an upright position. Supernatant was recovered by centrifugation at 5000 rpm for 10 minutes at 4°C. Plasma was aliquot (0.250 µL each) stored at -60°C till used for ethanol assay.

All the samples were separated, aliquotted, stored and analyzed at the Biochemistry Laboratory of the College of Medicine, Jouf University, Saudi Arabia.

5.6.4. EnEth Assay

EnEth was quantitatively assayed using a commercially available enzymatic colorimetric kit (Cat# E-BC-K891-M, Elabscience, Houston, Texas, USA). The assay has a detection range of 0.27-10.0 µmol/mL and the sensitivity is 0.27 µmol/mL. It is based on oxidative dehydrogenation of ethanol to acetaldehyde by ethanol dehydrogenase and NAD^+ that produces NADH. NADH, with help of the electron mediator, 1-methoxy-5-methylphenazium methylsulfate (1-mPMS), transfers electrons to the tetrazolium salt chromogen, the water-soluble tetrazolium salt-8 (WST-8) to produce the yellow formazan product, which has a characteristics absorption peak at 450 nm. Therefore, ethanol content can be quantified by measure the OD value at 450 nm. Enzymatic colorimetric assays are known for their extreme

sensitivity, specificity and accuracy, even compared to the most sophisticated approaches, e.g., mass spectroscopy and HPLC.

5.6.4.1. Assay Procedure

a. Standard wells: 40 µL aliquot of each standard concentration (0.0 – 8.0 µmol/mL) was dispensed into their corresponding wells of a 96-well microplate, as duplicates.

b. Sample wells: 40 µL aliquot of each sample was dispensed into sample well, as duplicates.

c. 160 µL aliquot of the reaction working solution [composed of reagents 1 (buffer A), working reagent 2 (working enzyme reagent dissolved in 180 µL distilled water), reagent 3 (buffer B), reagent 4 (working substrate solution dissolved in 170 µL distilled water), and reagent 5 (chromogenic agent); at a ratio of 80: 1: 37: 2: 8 v/v ratio] was dispensed into each well.

d. The microplate was horizontally shaken for 10 seconds, and the initial OD value was measured at 450 nm with the ELISA microplate reader (Multiskan FC microplate, Catalog 51119000, ThermoFisher Scientific, US), and was recorded as A1 (complete within 2 min).

e. The plate was incubate at 37^{o}C, away from light, for 10 min, and OD value was measured again at 450 nm, and was recorded as A2.

f. The net change in OD was calculated as ΔA = A2- A1. These net OD values were applied against the known ethanol standard concentration to construct the standard curve **[Figure 2]**, into which the samples' OD values were applied to extract samples' ethanol concentrations from the linear portion of the graph.

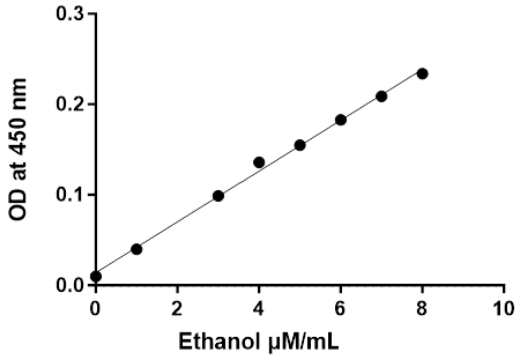


Figure 2. The standard curve constructed for calculation of ethanol content of the participants' saliva and plasma

5.7. Parameters/ Variables Studied

The EnEth concentration was correlated to demographics (age, gender), anthropometrics (waist circumference and BMI) and oral status of the participants.

5.8. Statistical analysis

Data was analysed using Statistical Package for Social Sciences version 22 (IBM SPSS statistics version 22, License Authorization Wizard. Ink, Chicago, USA). Data analysis is presented through tables and descriptive methods (frequency, mean and standard deviation). A chi-square test was used for categorical variables, and an independent t-test was applied for continuous variables. To assess the linear relationship among serum and salivary ethanol, Pearson's correlation coefficient was done. To evaluate diagnostic test accuracy of serum and salivary ethanol levels, Receiver Operating Characteristic (ROC) curve was done. Statistical significance was considered at $P \leq 0.05$.

6. RESULTS

6.1. Comparative analysis of demographic, anthropometric, and oral health parameters between the groups:

The mean age of the controls was 28.42±8.15, while the study group had a higher mean age of 34.98±11.31 years. Age distribution analysis revealed a statistically significant difference (P=0.033) among the groups, with a larger proportion of patients in the older age categories (46–50 years and 51–55 years) in the study group as compared to controls.

The gender distribution was nearly equal in both groups, with males comprising 50.9% of the controls and 49.1% of the study group, while females accounted for 49% of the controls and 51% of the study group. There was no statistically significant difference in gender distribution between the groups (P=0.999).

BMI analysis showed that the mean BMI was higher in study group (24.97±4.78) than in controls (22.34±3.57). The difference was statistically significant (P=0.015), with a greater proportion of patients (85.7%) falling into the obese category (BMI ≥ 30) compared to controls (14.3%).

The mean waist circumference was significantly higher in study group (91.58±14.30) than in controls (82.74±14.82) (P<0.001). A large proportion of patients (79.3%) exceeded the defined waist circumference thresholds (≥88cm for women and ≥102 cm for men) compared to controls (20.7%).

In the study group, 3.8% presented with fluorosis, 1.9% with dental erosion, and 1.9% with oral mucosal lesions (OML). No cases of trauma were recorded in either group.
The DMFT index score in the study group exhibited a mean score of 5.09±5.50. 81.1% of the patients had a DMFT score greater than 00, while 18.9% had a score of 00.

Table 1 shows comparative analysis of demographic, anthropometric, and oral health parameters between controls and study group.

6.2. Comparative analysis of serum and salivary variables between controls and study groups:

The overall mean serum ethanol levels were significantly higher in the study group (0.06 ± 0.018 μM/mL) compared to controls (0.033 ± 0.017 μM/mL), with a highly significant difference ($P < 0.001$). Similarly, salivary ethanol levels were elevated in the study group (0.033 ± 0.02 μM/mL) compared to controls (0.024 ± 0.01 μM/mL), with a significant P-value of 0.005.

Age-wise comparison revealed that in the 21–25 years category, serum ethanol levels in the study group were significantly higher (0.06 ± 0.018 μM/mL) than in controls (0.033 ± 0.017 μM/mL, $P < 0.001$), whereas salivary differences were not statistically significant. For the 26–30 years group, salivary ethanol levels showed significant elevation in the study group (0.053 ± 0.022 μM/mL) compared to controls (0.02 ± 0.014 μM/mL, $P = 0.022$). In the 31–35 years age group, serum ethanol levels were significantly higher in the study group (0.084 ± 0.022 μM/mL) than controls (0.044 ± 0.023 μM/mL, $P = 0.049$), while salivary differences were non-significant. Significant differences in serum ethanol levels were also observed in the 46–50 years age group, with the study group showing higher values (0.054 ± 0.012 μM/mL) compared to controls (0.017 μM/mL, $P = 0.028$).

Gender-wise comparison showed that both males and females in the study group exhibited significantly elevated serum and salivary ethanol levels compared to their control counterparts ($P < 0.001$ for serum and $P < 0.05$ for salivary).

For different BMI categories, among participants with BMI < 18.5, both serum ($P = 0.001$) and salivary ($P = 0.006$) ethanol levels were significantly higher in the study group than controls. Similarly, for BMI between 18.5–24.9 and 25–29.9, significant differences were noted in both serum and salivary ethanol levels.

For waist circumference, significant differences in serum levels were observed in individuals with waist circumference < 88 cm for women or < 102 cm for men ($P < 0.001$). However, salivary ethanol levels in this category were not significantly different.

For DMFT index score, the study group exhibited significantly higher serum and salivary ethanol levels for participants with DMFT > 0 (0.061 ± 0.021 and 0.033 ± 0.022 μM/mL respectively, $P < 0.001$) compared to the participants with DMFT = 0 (0.037 ± 0.020 and 0.025 ± 0.013 μM/mL respectively, $P < 0.001$).

Table 2 shows comparison of serum and salivary ethanol between control and study groups across demographic and clinical variables.

6.3. Correlation of serum and salivary ethanol levels across groups:

The correlation between serum and salivary ethanol levels was assessed using Pearson's correlation coefficient (r). The overall correlation for the entire sample (n = 106) was found to be statistically significant, with a moderate positive correlation (r = 0.286, P = 0.003). This indicates that as serum ethanol levels increased, there was a corresponding increase in salivary ethanol levels. When the analysis was stratified by groups, control group exhibited a stronger positive correlation between serum and salivary ethanol levels (r = 0.398, P = 0.003), suggesting a more pronounced relationship in this group. Conversely, study group showed a weak and statistically non-significant correlation (r = 0.058, P = 0.678), indicating that serum and salivary ethanol levels in this group were not closely associated. **(Table 3)**.

6.4. ROC curve analysis of serum and salivary ethanol levels for diagnostic accuracy:

The ROC curve was generated to evaluate the diagnostic performance of serum ethanol and salivary ethanol levels. The ROC curve for serum ethanol (blue line) showed superior sensitivity and specificity [Sensitivity = 90.6%, Specificity = 79.2%, and area under the curve (AUC) = 0.857 ± 0.038 (upper/lower bound = 0.782-0.931)], using the nonparametric approach, at asymptotic 95% CI (P < 0.001) at a cut-off level of 0.0405 μM/mL] compared to salivary ethanol (green line) [Sensitivity = 52.8%, Specificity = 67.9%, and AUC = 0.633 ± 0.054 (upper/lower bound = 0.527/0.740)], using the nonparametric approach, at asymptotic 95% CI (P = 0.018) at a cut-off level of 0.0285 μM/mL]. The serum ethanol curve demonstrated better discrimination with a larger AUC, indicating its higher diagnostic accuracy in distinguishing between the groups. The salivary ethanol curve, while less steep, still demonstrated moderate diagnostic utility, with a fair sensitivity and specificity. The reference line (golden diagonal) represents a random classification baseline, and both biomarkers outperformed this reference. These findings suggest that serum ethanol levels provide a more reliable diagnostic indicator compared to salivary ethanol levels, although salivary ethanol still holds potential as a non-invasive biomarker **[Figure 3]**.

7. DISCUSSION

The findings of this study provide strong evidence to reject the null hypothesis.

This study marks a significant advancement by pioneering the use of saliva as a biological fluid sample to assess EnEth levels and their correlation with blood EnEth levels. Saliva, being non-invasive and readily accessible, offers a practical alternative to traditional blood sampling methods. By demonstrating its feasibility as a diagnostic fluid, the research highlights the potential of non-invasive biomarkers and establishes a foundation for exploring oral-systemic health relationships.

Focusing on periodontitis - a chronic inflammatory disease driven by microbiome interactions - the study examines how microbial disruptions contribute to ethanol production and disease pathology. EnEth emerges as a promising biomarker for dysbiosis, providing a novel approach to monitoring disease progression. By linking EnEth levels to the pathophysiology of periodontitis and its systemic implications, this research underscores the significant role of microbial composition in both oral and systemic health, paving the way for innovative, non-invasive diagnostic methods.

7.1. Methods to measure EnEth

Accurately measuring EnEth levels has been a persistent challenge in clinical and research settings due to the inherent instability of ethanol in biological samples. Ethanol can continue to be produced in vitro through microbial activity within the sample, which can skew results if not meticulously controlled. However, advancements in analytical methods have significantly improved the reliability of EnEth measurement in different biological samples. These improvements offer a more practical and cost-effective approach for evaluating individual variations in EnEth production and their implications for health. In the current study, we utilized enzymatic colorimetric technique to evaluate EnEth levels. This technique involves reagents or enzymes such as alcohol dehydrogenase that react with ethanol to produce measurable products. This method is valued for its simplicity, speed, and affordability, making it ideal for population-wide studies. However, proper sample preparation is essential to prevent microbial fermentation after sample collection, which could artificially elevate ethanol levels.

ROC curve analysis revealed serum ethanol as a strong diagnostic marker to differentiate healthy controls from dental patients, with a sensitivity of 90.6%, specificity of 79.2%, and an AUC of 0.857 ± 0.038 (95% CI: 0.782–0.931, $P < 0.001$) at a cut-off of 0.0405 μM/mL. These findings align with Pay JB and Shaw AM, who noted serum's reliability in reflecting systemic changes, particularly in inflammatory conditions [19]. Salivary ethanol,

while less reliable, showed moderate diagnostic potential with a sensitivity of 52.8%, specificity of 67.9%, and an AUC of 0.633 ± 0.054 (95% CI: 0.527–0.740, P = 0.018) at a cut-off of 0.0285 μM/mL. Variations in salivary flow, composition, and microbial activity may account for its reduced sensitivity and specificity, as highlighted by Kaufman E and Lamster IB [20]. The superior accuracy of serum ethanol underscores its diagnostic value, while salivary ethanol offers a complementary, non-invasive alternative in clinical practice.

7.2. Comparison of Serum and Salivary Ethanol Concentrations

The study found significantly elevated serum and salivary ethanol levels in patients with PD compared to healthy controls, with marked differences attributed to oral microbial dysbiosis and systemic metabolic imbalances enhancing microbial fermentation. Healthy controls exhibited low but measurable EnEth levels, aligning with prior studies indicating baseline ethanol production from low-level gastrointestinal fermentation processes [21]. Data from previous studies show variability in EnEth levels, with breath ethanol values ranging from 0.0 to 0.082 mg/dL and venous blood ethanol concentrations averaging 0.027 mg/dL in healthy individuals [22]. A broader study reported mean EnEth levels of 0.14 ± 0.35 mg/dL, with a maximum of 1.53 mg/dL [21]. Higher EnEth levels in PD patients suggest microbial dysbiosis and associated inflammatory processes in PD significantly influence ethanol production. Comparative studies link increased microbial diversity and biomass in PD to higher ethanol production, highlighting PD as both a result and amplifier of microbial imbalances [16].

Although there is no direct data in the literature comparing salivary and blood ethanol levels in patients with PD, indirect comparisons can be drawn from studies on other chronic inflammatory conditions. It is well-known that EnEth levels are generally higher in individuals with metabolic disturbances, obesity, and diabetes - conditions that are also recognized as risk factors for PD. Similarly, research on gastrointestinal disorders such as inflammatory bowel disease (IBD) highlights a pattern of microbial dysbiosis and elevated ethanol levels due to an increased presence of ethanol-producing bacteria and fungi. These conditions, marked by microbial dysbiosis and ethanol-producing bacteria, exhibit elevated ethanol levels contributing to inflammation and systemic effects. For instance, non-alcoholic steatohepatitis (NASH) patients show increased gut-derived ethanol linked to liver inflammation, while diabetes studies reveal higher ethanol levels unrelated to glycemic control, driven by microbial shifts [12].

It is worth noting that in one case, ABS was described for the first time due to oral *Candida albicans* colonization, but mostly due to *Streptococcus* and *Klebsiella pneumoniae* bacteria from PD lesions, both demonstrating higher ethanol-producing capabilities than fungi [23].

7.3. Correlation between Serum and Salivary Ethanol levels

The study revealed a moderate positive correlation between serum and salivary ethanol concentrations overall ($r = 0.286$, $p = 0.003$), suggesting shared influences from microbial fermentation and metabolic processes. This correlation was notably stronger in the control group ($r = 0.398$, $p = 0.003$) than in the study group ($r = 0.058$, $p = 0.678$), indicating that PD disrupts the relationship between systemic and local ethanol levels. The stronger correlation in controls may reflect a balanced oral microbiome, enabling consistent ethanol distribution across serum and saliva, as supported by prior research highlighting the role of a healthy microbiome in metabolic regulation [7]. In contrast, the disrupted correlation in PD participants could result from altered microbial activity or metabolic pathways linked to oral dysbiosis. The complex interactions among pathogenic species in PD may interfere with ethanol production and distribution, reflecting the metabolic imbalances typical of dysbiotic states [7].

PD is known to share bidirectional links with gastrointestinal disorders, where chronic inflammation in the oral cavity or intestine mutually influences the other. Both systems are part of the interconnected digestive ecosystem, maintaining balance under physiological conditions but prone to inflammatory cascades when dysbiosis occurs [7]. The elevated EnEth levels observed in PD patients may stem from similar microbial and inflammatory mechanisms seen in gastrointestinal disorders. Chronic inflammatory conditions like PD likely share a common feature of dysbiosis-driven ethanologenesis, supported by microbial shifts that parallel those observed in other inflammatory diseases. These findings underscore the systemic impact of microbial imbalances and their role in the pathophysiology of chronic conditions.

7.4. Correlation with Demographics, Anthropometrics, and Oral Health Behaviour

7.4.1. Demographic Influences

7.4.1.1. Age

The mean age of participants in the study group (34.98 ± 11.31 years) was significantly higher than that of the controls (28.42 ± 8.15 years). Stratified analysis revealed a

higher proportion of patients aged 46–50 years (87.5%) compared to controls (12.5%), aligning with the understanding that aging is associated with cumulative microbial exposure, which exacerbates oral health issues such as PD [24]. Periodontitis becomes more prevalent and severe with age, potentially due to the accumulation of bacterial biofilms, decreased immune function, and poor oral hygiene habits [24].

Serum ethanol levels were notably higher in patients aged 31–35 years and 46–50 years compared to controls, while salivary ethanol levels showed significant differences in the 26–30 age group. These findings suggest age-related shifts in oral and gut microbial ecosystems and metabolic activities, potentially influenced by lifestyle factors like diet and oral hygiene [25]. A decline in the efficiency of ADH enzymes with age may also contribute to higher serum ethanol levels, as reduced metabolism allows ethanol concentrations to persist longer in the bloodstream [25]. Interestingly, no significant age-related differences were observed in salivary ethanol concentrations, indicating that salivary ethanol may be less sensitive to age-related changes compared to serum ethanol.

These findings suggest that age is a critical factor in periodontitis risk, possibly due to a combination of biological aging processes and lifestyle factors. Consequently, the significantly higher mean age in the periodontitis group in our study supports the hypothesis that age-related immune and systemic health changes may predispose individuals to dysbiosis and subsequent PD.

Al-Awadhi A et al. conducted a study in the United Arab Emirates to demonstrate the endogenous levels of blood ethanol in different subsets of the population. No significant difference was attributed to age, gender, and nationalities of the participants [26]. Similar results were replicated by Ragab AR et al. in the Saudi Arabian population [21].

7.4.1.2. Gender

In this study, no significant differences in gender distribution were found with nearly equal proportions of males and females in both groups. This suggests that the observed differences in other parameters, such as BMI and oral health, are independent of gender.

Gender-wise comparison showed that both males and females in the study group exhibited significantly elevated serum and salivary ethanol levels compared to their control counterparts. A study by Kezer CA et al. have found that females may exhibit higher ethanol retention and slower metabolism rates, possibly due to differences in ADH activity and body composition, including higher body fat percentage [27]. Nair S et al. in a study involving NASH patients found raised levels of breath alcohol concentration in obese and females, but

the latter was not significant [22]. These gender-based microbial differences could contribute to the observed differences in ethanol levels.

7.4.2. Anthropometrics Correlations

7.4.2.1. BMI

Participants in study group had a significantly higher mean BMI than controls. The obesity category showed marked disparities, with 85.7% of patients versus 14.3% of controls falling in this range. Patients in the study group exhibited significantly higher BMI compared to controls, reinforcing the well-established association between obesity and PD [28]. The role of obesity in modulating oral microbial composition and its impact on PD progression is further supported by studies identifying specific subgingival microbial signatures in obese individuals. These signatures, characterized by reduced microbial diversity may contribute to sustained periodontal inflammation and reduced treatment efficacy [28]. A plausible biological model suggests that adipose tissue from individuals with obesity secretes inflammatory mediators which cause a generalized inflammatory state resulting in alveolar bone loss [28].

Serum ethanol levels were significantly higher in study group across all BMI categories, except for those with BMI ≥ 30, where the difference was not statistically significant. Salivary ethanol levels were significantly elevated in study group across all BMI categories except for the participants <18.5. These findings suggest a complex relationship between BMI and ethanol production, where different individuals with different BMI may experience altered microbial activity due to systemic and metabolic imbalances [16].

Obesity is intrinsically linked to systemic conditions such as NAFLD, diabetes, and metabolic syndrome, all of which contribute to microbial dysbiosis and heightened inflammatory states [22]. These systemic imbalances can exacerbate oral conditions, including PD, through mechanisms such cytokine-mediated inflammation [16]. This supports the idea that systemic health conditions may indirectly promote a microbial environment favoring ethanol production, compounding the effects of local dysbiosis.

Additionally, the study observed distinct ethanol production patterns among underweight individuals, characterized by reduced salivary ethanol levels. This aligns with findings by Chanda D and De D who noted that lower BMI individuals often lack fermentative microbial species prevalent in obese populations [29].

7.4.2.1. Waist Circumference

The mean waist circumference was significantly higher in study group compared to controls, with 79.3% of individuals exceeding risk thresholds belonging to the study group.

This disparity highlights the critical role of central obesity, measured through waist circumference, as a risk factor for systemic and oral health issues. Elevated waist circumference is a reliable anthropometric marker of central adiposity, often associated with metabolic syndrome, systemic inflammation, and microbial dysbiosis, which collectively predispose individuals to oral diseases and other health complications [25]. While serum and salivary ethanol levels were higher in patients with elevated waist circumference, the differences were not statistically significant (except for individuals with waist circumference < 88 cm for women or < 102 cm for men), reflecting the complexity of the relationship between central obesity, microbial activity, and ethanol production. In this study, the higher waist circumference observed in study group supports the hypothesis that obesity and abdominal fat may contribute to both systemic and localized inflammatory responses, thereby influencing endogenous ethanol production.

The observed associations between waist circumference, microbial dysbiosis, and ethanol production highlights the potential of waist circumference as a dual-purpose clinical marker. It not only serves as an anthropometric measure of obesity but also reflects underlying microbial health. The elevated ethanol levels in patients with higher waist circumference suggest that waist circumference could inform clinical assessments of microbial health and metabolic risks. Consequently, integrating waist circumference measurements into routine health evaluations could provide valuable insights into the predisposition for endogenous ethanol production and associated inflammatory and dysbiotic conditions.

7.5. Oral Status

Although the prevalence of fluorosis (3.8%), erosion (1.9%), and oral mucosal lesions (1.9%) in patients was minimal, they highlight localized oral health concerns in the study group.

Patients exhibited a mean DMFT score of 5.09 ± 5.50 with 81.1% having a score greater than 0, highlighting a significant oral disease burden potentially driven by poor oral hygiene, and dietary habits. Higher serum ethanol levels in participants with DMFT > 0, suggest systemic implications of dental caries on EnEth production. Salivary ethanol levels differ significantly between groups, and this trend suggests that local microbial fermentation may lead to ethanol accumulation, subsequently absorbed into systemic circulation. Elevated serum ethanol levels in caries-affected individuals may result from an imbalance in the oral microbiome.

The relationship between oral health and systemic conditions, particularly gastrointestinal and liver diseases, is increasingly recognized as a critical area of study. The number

of missing teeth serves as a robust barometer of overall oral health, reflecting the cumulative impact of inflammatory and infectious conditions in the oral cavity [25]. This metric is widely acknowledged as a primary indicator of oral health status. Studies have demonstrated that individuals with chronic conditions such as IBD, diabetes, and obesity exhibit a higher prevalence of tooth decay and PD. For example, research by Koutsochristou V et al. reported increased rates of dental caries and PD among individuals with chronic illnesses compared to their healthy counterparts, even when oral hygiene indicators were comparable [30].

Emerging evidence underscores the significant role of the oral microbiota in systemic health. An imbalance in the "oral–intestinal" axis, characterized by increased oral bacterial translocation to the gut, triggers inflammatory responses through immune system activation. Epidemiological studies have established associations between oral health and systemic diseases, including cardiovascular diseases, diabetes, and NAFLD. Missing or untreated teeth, as indicators of poor oral health, correlate with these conditions through shared risk factors such as obesity, gut microbiota dysbiosis, and chronic inflammation. Chronic oral inflammation and microbial imbalances may also influence gastrointestinal health and vice versa, as evidenced by the complex interactions between PD, IBS, and NAFLD [25].

Dietary habits and lifestyle factors, as well as high-sugar diets or processed foods, can play a role in the creation of both oral disorders and gastrointestinal problems. These habits can influence the oral and gastrointestinal microbiome, contributing to microbial imbalances. Several factors cause gut dysbiosis, e.g., diets and sweetening agents can increase opportunistic gut colonization by oral bacteria. These factors can influence the oral and gastrointestinal microbiome, contributing to microbial imbalances. High-sugar diets and processed foods contribute to both oral disorders (e.g., dental caries, PD) and gastrointestinal problems. These diets can promote microbial imbalances that negatively impact health [31].

8. SUMMARY AND CONCLUSIONS

Hence to summarize, the significant increase in serum and salivary ethanol concentrations observed in the study group underscores EnEth's potential role as a biomarker for microbial dysbiosis and its broader implications for oral and systemic health. These findings suggest that monitoring EnEth levels could provide critical insights into the complex relationship between periodontal disease, dysbiosis, and overall health outcomes. In this context, salivary ethanol emerges as a promising proxy biomarker for assessing disease severity and guiding individualized treatment strategies, advancing both dental and medical care.

In conclusion, this study revealed significant differences in endogenous ethanol concentrations between patients with periodontal disease and healthy controls, influenced by age, BMI, waist circumference, and dental caries. While salivary ethanol offers a non-invasive marker, serum ethanol exhibits greater diagnostic accuracy. These findings underscore the importance of systemic factors in periodontitis and suggest further exploration of ethanol as a biomarker for its metabolic and microbial dimensions. While salivary ethanol provides a non-invasive biomarker, serum ethanol exhibits greater diagnostic accuracy, warranting further exploration of its clinical utility. Further research is needed to explore the underlying microbial mechanisms and the broader implications of ethanol production in periodontal diseases.

9. REFERENCES

1. Tameez Ud Din A, Alam F, Tameez-Ud-Din A, Chaudhary FMD. Auto-Brewery Syndrome: A Clinical Dilemma. Cureus. 2020;12(10):e10983. doi: 10.7759/cureus.10983.
2. Logan BK, Jones AW. Endogenous ethanol 'auto-brewery syndrome' as a drunk-driving defence challenge. Med Sci Law. 2000;40(3):206-15. doi: 0.1177/002580240004000304.
3. Paramsothy J, Gutlapalli SD, Ganipineni VDP, Okorie IJ, Ugwendum D, Piccione G, Ducey J, Kouyate G, Onana A, Emmer L, Arulthasan V, Otterbeck P, Nfonoyim J. Understanding auto-brewery syndrome in 2023: a clinical and comprehensive review of a rare medical condition. Cureus. 2023;15(4):e37678. doi: 10.7759/cureus.37678.
4. Edenberg HJ. The genetics of alcohol metabolism: role of alcohol dehydrogenase and aldehyde dehydrogenase variants. Alcohol Res Health. 2007;30(1):5-13. PMID: 17718394; PMCID: PMC3860432.
5. Jones AW, Mårdh G, Anggård E. Determination of endogenous ethanol in blood and breath by gas chromatography-mass spectrometry. Pharmacol Biochem Behav. 1983;18 Suppl 1:267-72. doi: 10.1016/0091-3057(83)90184-3.
6. Hafez EM, Hamad MA, Fouad M, Abdel-Lateff A. Auto-brewery syndrome: Ethanol pseudo-toxicity in diabetic and hepatic patients. Hum Exp Toxicol. 2017;36(5):445-450. doi: 10.1177/0960327116661400.
7. Sedghi L, DiMassa V, Harrington A, Lynch SV, Kapila YL. The oral microbiome: Role of key organisms and complex networks in oral health and disease. Periodontol 2000. 2021;87(1):107-131. doi: 10.1111/prd.12393.
8. Willis JR, Gabaldón T. The human oral microbiome in health and disease: from sequences to ecosystems. Microorganisms. 2020;8(2):308. doi: 10.3390/microorganisms8020308.

9. Bui FQ, Almeida-da-Silva CLC, Huynh B, Trinh A, Liu J, Woodward J, Asadi H, Ojcius DM. Association between periodontal pathogens and systemic disease. Biomed J. 2019;42(1):27-35. doi: 10.1016/j.bj.2018.12.001.
10. Ladkin RG, Davies JN. Rupture of the stomach in an African child. Br Med J. 1948;1(4552):644. doi: 10.1136/bmj.1.4552.644.
11. Iwata, K. A review of the literature on drunken syndromes due to yeasts in the gastrointestinal tract. In Yeasts and Yeast-Like Microorganisms in Medical Science, Proceedings of the Second International Specialized Symposium on Yeasts, 1972, Tokyo, Japan; Iwata, K., Ed.; University of Tokyo Press: Tokyo, Japan, 1976; pp. 260–268.
12. Patel P, Patel D, Gutlapalli SD, Okorie IJ, Onana AE, Ugwendum D, Arrey Agbor DB, Munoh Kenne F, Otterbeck P, Nfonoyim J. The associations of auto-brewery syndrome and diabetes mellitus: a literature review and clinical perspective. Cureus. 2023;15(7):e41924. doi: 10.7759/cureus.41924.
13. Ruiz-Hernández V, Roca MJ, Egea-Cortines M, Weiss J. A comparison of semi-quantitative methods suitable for establishing volatile profiles. Plant Methods. 2018;14:67. doi: 10.1186/s13007-018-0335-2.
14. Poklis A, MacKell MA. Use of gas chromatography and alcohol dehydrogenase in a routine procedure for the determination of ethanol in postmortem blood. Journal of Analytical Toxicology 1979;3(5):183–186. doi: 10.1093/jat/3.5.183.
15. Kumar PS. From focal sepsis to periodontal medicine: a century of exploring the role of the oral microbiome in systemic disease. J Physiol. 2017;595(2):465-476. doi: 10.1113/JP272427.
16. Kuraji R, Shiba T, Dong TS, Numabe Y, Kapila YL. Periodontal treatment and microbiome-targeted therapy in management of periodontitis-related nonalcoholic fatty liver disease with oral and gut dysbiosis. World J Gastroenterol 2023;29(6):967-996. doi: 10.3748/wjg.v29.i6.967.
17. Available at ski2156-sup-0002-suppl-data.pdf.
18. Başıbüyük GÖ, Ayremlou P, Saeidlou SN, Ay F, Dalkıran A, Simzari W, Vitályos GÁ, Bektaş Y. A comparison of the different anthropometric indices for assessing malnutrition among older people in Turkey: a large population-based screening. J Health Popul Nutr. 2021;40(1):13. doi: 10.1186/s41043-021-00228-z.
19. Pay JB, Shaw AM. Towards salivary C-reactive protein as a viable biomarker of systemic inflammation. Clin Biochem. 2019;68:1-8. doi: 10.1016/j.clinbiochem.2019.04.006.

20. Kaufman E, Lamster IB. The diagnostic applications of saliva--a review. Crit Rev Oral Biol Med. 2002;13(2):197-212. doi: 10.1177/154411130201300209.
21. Ragab AR, Maha Al-Mazroua K, Afify MM, Al Saeed I, Katbai C. Endogenous ethanol production levels in Saudi Arabia residents. J Alcohol Drug Depend 2015;3(3). doi: 10.4172/2329-6488.1000211.
22. Nair S, Cope K, Risby TH, Diehl AM. Obesity and female gender increase breath ethanol concentration: potential implications for the pathogenesis of non-alcoholic steatohepatitis. Am J Gastroenterol. 2001;96(4):1200-4. doi: 10.1111/j.1572-0241.2001.03702.x.
23. Takahashi G, Hoshikawa K, Kan S, Akimaru R, Kodama Y, Sato T, Kakisaka K, Yamada Y. Auto-brewery syndrome caused by oral fungi and periodontal disease bacteria. Acute Med Surg. 2021;8(1):e652. doi: 10.1002/ams2.652.
24. López R, Smith PC, Göstemeyer G, Schwendicke F. Ageing, dental caries and periodontal diseases. J Clin Periodontol. 2017;44 Suppl 18:S145-S152. doi: 10.1111/jcpe.12683.
25. Rotaru M, Singeap AM, Ciobica A, Huiban L, Stanciu C, Romila L, Burlui V, Mavroudis I, Trifan A. Oral health and "modern" digestive diseases: pathophysiologic and etiologic factors. Biomedicines. 2024;12(8):1854. doi: 10.3390/biomedicines12081854.
26. Al-Awadhi A, Wasfi IA, Al Reyami F, Al-Hatali Z. Autobrewing revisited: endogenous concentrations of blood ethanol in residents of the United Arab Emirates. Sci Justice. 2004;44(3):149-52. doi: 10.1016/S1355-0306(04)71707-4.
27. Kezer CA, Simonetto DA, Shah VH. Sex differences in alcohol consumption and alcohol-associated liver disease. Mayo Clin Proc. 2021;96(4):1006-1016. doi: 10.1016/j.mayocp.2020.08.020.
28. Martinez-Herrera M, Silvestre-Rangil J, Silvestre FJ. Association between obesity and periodontal disease. A systematic review of epidemiological studies and controlled clinical trials. Med Oral Patol Oral Cir Bucal. 2017;22(6):e708-e715. doi: 10.4317/medoral.21786.
29. Chanda D, De D. Meta-analysis reveals obesity associated gut microbial alteration patterns and reproducible contributors of functional shift. Gut Microbes. 2024;16(1):2304900. doi: 10.1080/19490976.2024.2304900.
30. Koutsochristou V, Zellos A, Dimakou K, Panayotou I, Siahanidou S, Roma-Giannikou E, Tsami A. Dental caries and periodontal disease in children and adolescents with inflammatory bowel disease: A case-control study. Inflamm Bowel Dis. 2015;21(8):1839-46. doi: 10.1097/MIB.0000000000000452.

31. Rinninella E, Raoul P, Cintoni M, Franceschi F, Miggiano GAD, Gasbarrini A, Mele MC. What is the healthy gut microbiota composition? a changing ecosystem across age, environment, diet, and diseases. Microorganisms. 2019;7(1):14. doi: 10.3390/microorganisms7010014.

10. TABLES AND FIGURES

Table 1. Demographic, anthropometric and oral health behaviours characteristics of the healthy controls and participants with periodontal disease

Variables		Controls (n = 53)	Study (n = 53)	P
Age (in years)	Overall mean ± SD Range	28.42 ± 8.15 21-52	34.98 ± 11.31 28-55	--
	21-25	31(62.0%)	19(38.0%)	0.033, S
	26-30	6(60%)	4(40%)	
	31-35	3(37.5%)	5(62.5%)	
	36-40	7(63.6%)	4(36.4%)	
	41-45	4(30.8%)	9(69.2%)	
	46-50	1 (12.5%)	7(87.5%)	
	51-55	1 (16.7%)	5(83.3%)	
Gender	Males	28(50.9%)	27(49.1%)	0.999, NS
	Females	25(49%)	26(51%)	
BMI (in $kg/m^{2)}$	Overall mean ± SD Range	22.34 ± 3.57 17.8-33.6	24.97 ± 4.78 17.9-35.6	--
	≤ 18.5	8(66.7%)	4(33.3%)	0.015, S
	18.5 - 24.9	31(56.4%)	4(43.6%)	
	25 - 29.9	12(48%)	13(52%)	
	≥ 30	2(14.3%)	12(85.7%)	
Waist circumfer-ence (in cm)	Overall mean ± SD Range	82.74 ± 14.82 62.2 – 101.5	91.58 ± 14.30 66 - 112.4	--
	< 88 for women / < 102 for men	47(61%)	30(39%)	<0.001, S
	≥ 88 for women / ≥ 102 for men	6(20.7%)	23(79.3%)	
Oral status	Fluorosis	0 (0%)	2(3.8%)	--
	Erosion	0 (0%)	1(1.9%)	
	Trauma	0 (0%)	0(0%)	
	OML	0 (0%)	1(1.9%)	
DMFT index score	Overall mean ± SD (Range)	0 ± 0 (0-0)	5.09 ± 5.50	--
	= 0	0 (0%)	10 (18.9%)	
	> 0	0 (0%)	43 (81.1%)	

OML = Oral mucosal lesions
DMFT = Mean number of decayed, missing, and filled permanent teeth
BMI = Body mass index
S = Statistically significant
NS = Statistically non-significant

Table 2. Serum and salivary ethanol levels (µM/mL) for the healthy controls and participants with periodontal disease stratified for their age, gender, anthropometrics, and DMFT index score

Variables		Serum		P	Salivary		P
		Controls (n = 53)	**Study (n = 53)**		**Controls (n = 53)**	**Study (n = 53)**	
Overall mean ± SD		0.033 ± 0.017	0.06 ± 0.018	<0.001, S	0.024 ± 0.01	0.033 ± 0.02	0.005, S
Age (in years)	21-25	0.033 ± 0.017	0.06 ± 0.018	<0.001, S	0.024 ± 0.01	0.028 ± 0.017	0.317, NS
	26-30	0.037 ± 0.015	0.07 ± 0.031	0.083, NS	0.02 ± 0.014	0.053 ± 0.022	0.022, S
	31-35	0.044 ± 0.023	0.084 ± 0.022	0.049, S	0.016 ± 0.012	0.034 ± 0.029	0.369, NS
	36-40	0.026 ± 0.012	0.038 ± 0.019	0.251, NS	0.028 ± 0.017	0.041 ± 0.02	0.308, NS
	41-45	0.037 ± 0.025	0.068 ± 0.027	0.755, NS	0.026 ± 0.011	0.031 ± 0.019	0.661, NS
	46-50	0.017	0.054 ± 0.012	0.028, S	0.012	0.029 ± 0.017	0.338, NS
	51-55	0.055	0.057 ± 0.009	0.820, NS	0.032	0.048 ± 0.034	0.695, NS
Gender	Males	0.031 ± 0.017	0.059 ± 0.023	<0.001, S	0.022 ± 0.012	0.031 ± 0.22	0.049, S
	Females	0.037 ± 0.017	0.06 ± 0.021	<0.001, S	0.026 ± 0.013	0.044 ± 0.021	0.045, S
BMI (in kg/m^2)	< 18.5	0.034 ± 0.023	0.061 ± 0.019	0.001, S	0.025 ± 0.012	0.013 ± 0.01	0.006, S
	18.5 - 24.9	0.028 ± 0.008	0.063 ± 0.024	<0.001, S	0.024 ± 0.009	0.029 ± 0.001	0.197, S
	25 - 29.9	0.04 ± 0.01	0.06 ± 0.03	0.011, S	0.02 ± 0.013	0.04 ± 0.012	0.001, S
	≥ 30	0.04 ± 0.014	0.057 ±	0.248, NS	0.044 ± 0.022	0.056 ±	0.534, NS

			0.018			0.025	
Waist circum-ference (in cm)	< 88 for women / < 102 for men	0.03 ± 0.017	0.062 ± 0.022	<0.001, S	0.023 ± 0.011	0.023 ± 0.015	0.857, NS
	≥ 88 for women / ≥ 102 for men	0.042 ± 0.012	0.06 ± 0.022	0.075, NS	0.031 ± 0.019	0.047 ± 0.021	0.102, NS
DMFT index score	= 0	--	0.037 ± 0.020	<0.001, S	--	0.025 ± 0.013	<0.001, S
	> 0	--	0.061 ± 0.021		--	0.033 ± 0.022	

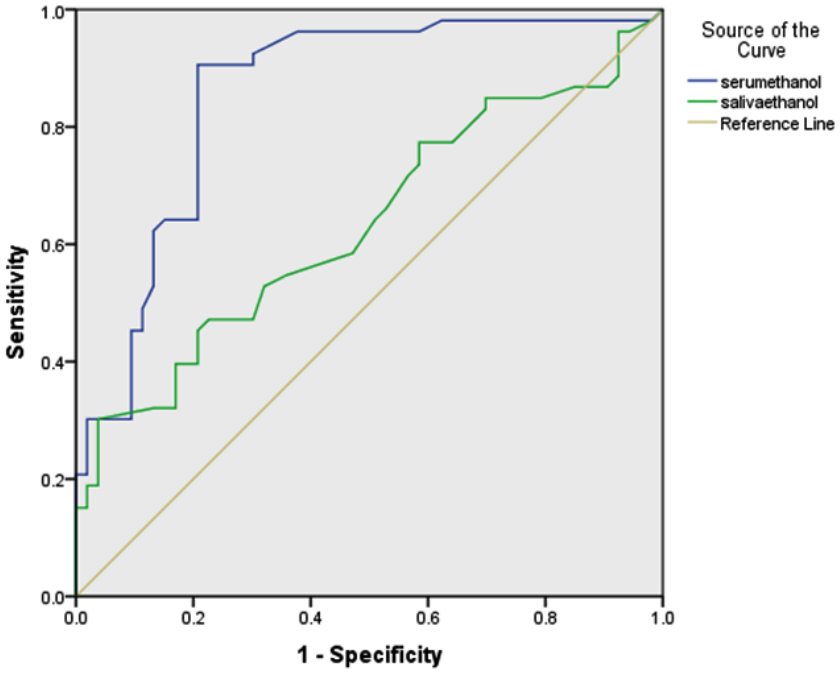
S = Statistically significant
NS = Statistically non-significant

Table 3. Pearson correlation coefficient (r) analysis between serum and salivary ethanol among the investigated groups

Group	r	P
Overall (n = 106)	0.286	0.003, S
Control group (n = 53)	0.398	0.003, S
Study group (n = 53)	0.058	0.678, NS

r = Pearson correlation
S = Statistically significant
NS = Statistically non-significant

Figure 3. ROC curve analysis of AUC to determine ability of each of serum and salivary ethanol levels to distinguish healthy controls from participants with periodontal disease



diagnostics

MDPI

Review

Exploring the Mechanisms and Association between Oral Microflora and Systemic Diseases

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Abstract: The scope of dentistry is ever-changing and dynamic in all fields of dentistry including periodontal health and disease. Recent studies show that oral health and systemic health are interdependent, particularly in the way that poor oral hygiene and periodontal health affect the systemic health of an individual and vice versa. Periodontal diseases are multifactorial in nature in which the role of bacterial infections is inevitable. Furthermore, high-throughput sequencing technologies have shed light on the dysregulation of the growth of oral microbial flora and their environment, including those that are associated with periodontitis and other oral and non-oral diseases. Under such circumstances, it becomes important to explore oral microbiota and understand the effects of periodontal pathogens in the pathogenesis of systemic diseases. In addition, it may strengthen our view that a better understanding of oral microbial flora and proper examination of the oral cavity may aid in the early diagnosis and possible treatment of systemic diseases and conditions. This will eventually lead to providing better care to our patients. Therefore, in this research, we attempt to outline the periodontal pathophysiology along with the role of periodontal pathogens in some commonly encountered systemic conditions.

Keywords: bacteria; diseases; pathogens; periodontitis; systemic

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1. Introduction

The oral cavity serves as a good medium for bacterial growth and it harbors a variety of microorganisms with approximately 500–700 prevalent taxa [1]. This microbial community is known as the oral microbiota, oral microflora, or oral microbiome [2]. However, its composition varies constantly throughout its life which is determined by a host of factors such as oral hygiene, dietary habits, the use of medications, host genetics, presence of exogenous microorganisms and some systemic factors [3]. With the advancements in isolation and culture techniques and the availability of more specific culture media, a better understanding of the coexistence of such complex polymicrobial communities as well as the role of local and systemic factors that govern/dictate the composition of oral microbiota was made possible [4].

For over a century, although it was assumed that oral diseases and systemic diseases were interrelated, there was no adequate scientific evidence [3]. However, as late as the

Review

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Role of Oral Microbiota in Carcinogenesis: A Short Review

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A strong and healthy microbiome is responsible for homeostasis between the host and microbiota which is necessary to achieve the normal functioning of the body. Dysbiosis provokes prevalence of pathogenic microbes, leading to alterations in gene expression profiles and metabolic processes. This in turn results in anomalous immune responses of the host. Dysbiosis may be associated with a wide variety of diseases like irritable bowel syndrome, coeliac disease, allergic conditions, bronchitis, asthma, heart diseases and oncogenesis. Presently, the links between oral microbial consortia and their functions, not only in the preservation of homeostasis but also pathogenesis of several malignancies have gained much awareness from the scientific community. The primary intent of this review is to highlight the dynamic role of oral microbiome in oncogenesis and its progression through various mechanisms. A literature search was conducted using multiple databases comprising of PubMed, Scopus, Google Scholar, and Cochrane electronic databases with keywords including microbiome, microbiota, carcinogenesis, tumorigenesis, and immunosuppression. Current and the past literature has pointed out the role of microorganisms in oncogenesis. It may be put forth that both the commensal and pathogenic strains of oral microbiome play an undeniably conspicuous role in carcinogenesis at different body sites.

Key Words Carcinogenesis, Immunosuppression therapy, Microbiota, Mouth

INTRODUCTION

The development of human beings after birth is characteristically viewed as an exclusive system of organ evolution. But perhaps we are missing a part of the picture. Humans are not mere individuals but a complex biological system harboring trillions of microbial cells [1,2]. Human body serves as a habitat for a wide array of microorganisms, which in conglomeration with their genetic matter constitute a comminity, referred to as the microbiome [2]. Human microbiome that may be depicted as an "essential organ" bears almost 100-fold more microbial genes than does the host genes [3-5]. Each organ or site of the body harbors a diverse population of pathogens that are dynamically milled alongside human development from birth through adolescence [4].

Human microbiome is known to colonize different sites such as skin, oral mucosa, respiratory tract, gastrointestinal (GI) tract, urogenital tract and so on [6]. Additionally, it is worthy to note that the composition of the microbiome and their function vary according to different sites, gender, ethnicity, and nutrition status of the host [7]. It is now widely accepted that these microbes are not just passive passengers but play a crucial role in normal growth, resistance to disease, and immune response. For instance, microbiota aid in vitamin biosynthesis protects against pathogens, influences innate immune responses, modulates the metabolic phenotype and regulates epithelial development [7]. Thus, the microflora helps in maintaining the homeostasis, thereby making normal functioning of the body achievable [6,7].

Just as microbiota is important in healthy functioning of the human body, it has a definitive role in dysfunction and disorders too [4]. Any disturbance in the homeostasis may result in dysbiosis, allowing some pathogens to become more prevalent and eventually leading to the diseases. Dysbiosis can alter host gene activity and metabolic processes, which in turn results in an anomalous immune response of the host [8]. Dysbiosis can contribute to the onset of a disease in several different ways. These include "gain of function dysbiosis",

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REVIEW

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Periodontitis as a Risk Factor for Breast Cancer – What We Know Till Date?

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Abstract

A healthy microbiome is important for human health because it exhibits a variety of functions in the human body wherein the microbiome dysbiosis can lead to a variety of diseases, including cancer. Recent advances in technology and cost reduction of sequencing have made it possible and much easier for researchers to investigate the role of the microbiome in carcinogenesis. Furthermore, modulation of microflora may serve as an effective adjunct to conventional anticancer therapy that is very important to improve the patient's quality of life. Additionally, microbiome biomarkers can also be used as a diagnostic tool for cancer. So far the association between oral microbial consortia and their interactions with the host in maintaining the human health and the pathogenesis of multiple cancers has gained much popularity in the scientific research community. While the interactions of oral microflora are better established in cancer- like gastric cancer, it is far less understood in others like breast cancer. Therefore, this review briefly outlines the current information on the role of oral microbiota in breast cancer with emphasis on the mechanisms of oral microflora induced carcinogenesis and discusses the emerging role of periodontitis as a risk factor for breast cancer. Clinical relevance; Periodontitis is a very common disease that is characterized by chronic polymicrobial infection and inflammation of gingiva. It might be associated as a risk factor for breast cancer. If this association is validated in large cohort studies, it would serve as a non-invasive biomarker for breast cancer.

Keywords: Breast- cancer- microbiome- microflora- oral

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Introduction

Humans are not mere individuals but a complex biological system harboring trillions of microbial cells (Parida and Sharma, 2019a; Singh et al., 2021). Human microbiome is the collective genome of all bacteria, archaea, protozoans, fungi, and viruses that inhabitants the human body which encodes nearly 100-fold more microbial genes when compared to the host genes (Parida and Sharma, 2019b; Manzoor et al., 2020; Bhatt et al., 2017). Each anatomical site of the human body exhibits a distinct and diverse microbial community that is dynamically shaped alongside human development from birth through adolescence (Manzoor et al., 2020). Human microbiome is known to colonize different sites such as the skin, the mucosa, respiratory tract, gastrointestinal tract, urogenital tract, etc (Manzoor et al., 2020). Experiments assessing gnotobiotic and germ-free mice suggest that this 'hidden and forgotten organ' provides important functions that affect cellular metabolism, inflammatory, neurological and immunologic functions (Manzoor et al., 2020; Bhatt et al., 2017; Eslami et al., 2020; Xavier et al., 2020; Tuominen and Rautava, 2021).

Just as microbiota is important in healthy functioning, it has a hand in many disorders (Manzoor et al., 2020). Dysbiosis, defined as a disturbance in the microbiome structure, may consist of processes not necessarily mutually exclusive, like the loss of beneficial microorganisms, proliferation of pathobionts, or harmful microorganisms, and general loss of microbial diversity (Garcia-Castillo et al., 2016). Therefore, in case of disrupted regulatory circuits of host controlling homeostasis, the symbiotic relationships gets hampered, leading to a wide array of ailments ranging from neurologic to metabolic and cardiovascular disorders as well as gastrointestinal disturbances (Garcia-Castillo et al., 2016; Helmink et al., 2019).

In recent years, researchers have focused in assessing the role of microbes in carcinogenesis (Eslami et al., 2020; Sharma et al., 2021). In the year 2018, there were more than 17 million new cases of human cancer, making cancer as one of the main causes of death worldwide (Ferlay et

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Review

Exploring an Association between Body Mass Index and Oral Health—A Scoping Review

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Abstract: Background: Basal metabolic index (BMI) is a unique anthropometric indicator used to define the relative amount of body fat on an individual's frame. There are many diseases and conditions associated with obesity and underweight. Recent research trials suggest that there is a significant association between oral health indicators and BMI as both are attributed to common risk factors such as dietary, genetic, socioeconomic, and lifestyle issues. Objectives: The main objective of this review paper is to emphasize the association between BMI and oral health with available literature evidence. Methodology: A literature search was conducted using multiple databases comprising of MEDLINE (via PubMed), EMBASE, and Web of Science. The terms used for the search were "body mass index", "periodontitis", "dental caries", and "tooth loss". Results: In total, 2839 articles were obtained from the analysis of the databases. Unrelated articles from the available full text of 1135 articles were excluded. The main reasons for excluding the articles were: they were dietary guidelines and policy statements. A total of 66 studies were finally included in the review. Conclusion: The presence of dental caries, periodontitis and tooth loss may be associated with a higher BMI or obesity, whereas, improved oral health might be associated with lower BMI. Promoting general and oral health should be a hand in hand feature, as common risk factors can be embattled.

Keywords: basal metabolic index; dental caries; inflammation; obesity; oral health; periodontitis

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1. Introduction

In the modern era, the most challenging community health issue is the growing number of overweight and obese individuals [1]. A recent study showed that between 1980 and 2014, the prevalence of obesity and overweight increased globally [2]. It is interesting to note that the WHO estimated that almost 2.5 billion persons over the age of 18 suffer from obesity and overweight in 2014 [2]. This is around a third of the entire world's population [2,3]. Between nations and regions within nations, the incidence varies greatly. Men are more likely to be overweight than women, while women are more likely to be obese [3]. In addition, obesity is currently ranked as the fifth biggest cause of death globally and the risk of death increases by 20–40% in overweight individuals, and it escalates to 200–400% in obese individuals. Every year, obesity and overweight cause the death of around 3.4 million people [2,4,5].

Obesity has been linked to a number of illnesses, including heart disease, musculoskeletal problems, hypertension, type 2 diabetes, and several cancers such as breast, prostate, liver, and colon cancer [6,7]. This adds to the burden of medical costs for obese individuals that are found to be 30% greater than for normal-weight peers [8]. Despite the

POSTER PRESENTATIONS (TOTAL 2)

CERTIFICATE

OF PARTICIPATION

This certificate is presented to

IDA Temple City Bhubaneswar Branch

Dr./Mr./Ms. DR. RAKHI ISSRANI

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